Intravascular Ultrasound–Guided Percutaneous Coronary Interventions: An Ongoing Odyssey?

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Editorial

Intravascular Ultrasound–Guided Percutaneous Coronary Interventions

An Ongoing Odyssey?

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Coronary angiography falls short in accurately delineating the anatomy of epicardial vessels because it provides only a 2-dimensional visualization of the lumen.[1] Moreover, angiographic lesion assessment is impeded in cases of diffuse disease of reference vessels, lesion foreshortening, and eccentricity, and the overlap of several arterial branches, as well. Conversely, intravascular ultrasound—a sound wave–based technology—provides superior spatial resolution of 80 to 150 μm and extends diagnostic information, enabling more precise assessment of lumen and vessel wall dimensions including atheroma burden and vessel remodeling.

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Intravascular ultrasound (IVUS) has been proposed for the assessment of lesion severity in cases of intermediate left main and non–left main lesions. In addition, IVUS has been used to guide percutaneous coronary interventions (PCI) by informing the operator of reference vessel dimensions, lesion length, and extent of calcification to plan the procedure. Finally, IVUS has been implemented to optimize stent deployment, and criteria have been developed such as the Multicenter Ultrasound Guided Stent Implantation (MUSIC)[2] and Angiography versus IVUS Optimization (AVIO)[3] criteria to this effect.

During the bare metal stent era, IVUS guidance was reported to reduce the risk of restenosis and repeat revascularization.[4] In contrast, the use of IVUS after drug-eluting stent (DES) implantation failed to improve clinical efficacy with IVUS guidance despite larger stent dimensions at the end of the procedure. Notwithstanding, some studies suggested a lower risk of stent thrombosis with IVUS-guided DES implantation owing to the detection of mechanical factors associated with stent thrombosis, including edge dissections, stent malapposition, and stent underexpansion.[5] More recently, the propensity score–matched comparison of IVUS guided with angiography-guided PCI of unprotected left main lesions (MAIN-COMPARE)[6] reported lower mortality, with IVUS guidance potentially related to a lower risk of sudden death and stent thrombosis.

Current American College of Cardiology Foundation/American Heart Associate PCI guidelines[7] consider IVUS as a potential diagnostic tool for the assessment of intermediate left main lesions, cardiac allograft vasculopathy (IIa, B), and the evaluation of the mechanism of in-stent restenosis (IIa, C). Furthermore, the guidelines give room to support coronary stent implantation particularly in cases of stent implantation in the left main coronary artery (IIb, B). However, the uptake of IVUS to guide PCI has been modest (<5% of procedures) at best since its introduction in the early 1990s.[8] Reasons for this restraint are the added complexity and prolongation of the procedure and a paucity of solid scientific data in support of IVUS-guided PCI. Previous randomized studies[2,3,9,10] were largely underpowered and enrolled low-risk patients in whom the potential benefit of intravascular imaging was predictably low. Several small observational studies reported conflicting results, and a recent systematic review summarizing these studies suggested a benefit of IVUS-guided PCI in terms of death and stent thrombosis without differences in myocardial infarction and target lesion revascularization.[11]

Against this background, Witzenbichler and colleagues[12] provide new evidence of a prespecified substudy of the Platelet Reactivity and Clinical Outcomes After Coronary Artery Implantation of Drug-eluting Stents (ADAPT) DES registry comparing clinical outcomes between IVUS-guided and angiography-guided PCI. In propensity-adjusted multivariable analysis, IVUS guidance was strongly associated with reduced rates of definite/probable stent thrombosis (adjusted hazard ratio, 0.40; 95% confidence interval, 0.21–0.73; P=0.003), myocardial infarction (adjusted hazard ratio, 0.66; 95% confidence interval, 0.49–0.88; P=0.004), and major adverse coronary events (adjusted hazard ratio, 0.70; 95% confidence interval, 0.55–0.88; P=0.003) at 1 year with the greatest benefit emerging among patients with acute coronary syndrome and complex lesions (eg, left main, bifurcation, multivessel PCI). The study has several notable strengths. First, ADAPT DES is the largest prospective IVUS study performed to date with 3349 patients undergoing IVUS-guided PCI and 5234 patients undergoing angiography-guided PCI. Second, the study was performed in the setting of an all-comers patient population with a considerable proportion of patients with high-risk clinical characteristics including diabetes mellitus (31%), acute coronary syndrome (55%), ST-elevation myocardial infarction (12%), and lesion subsets (14% bifurcation lesions, 4% left main, 25% 3-vessel disease). Third, the investigators used propensity-adjusted multivariable analyses in an attempt to minimize the risk of bias. Fourth, prespecified and clinical events committee–adjudicated clinical end points were implemented as for the primary end

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point, and, fifth, the investigators performed paired IVUS before and after the procedure in 60% of cases.

The following shortcomings deserve comment. The most prominent limitation of this observational study is the lack of randomization resulting in important differences in patient and lesion characteristics. IVUS patients were younger, had less previous coronary artery bypass graft surgery and 3-vessel disease, had a more extended duration of dual-antiplatelet therapy, and received new-generation DES more frequently. These differences indicate that IVUS assignment was not free from bias, and, despite using propensity-adjusted multivariable analyses, residual confounding factors cannot be excluded beyond a reasonable doubt. Along this line, important differences in clinical end points unrelated to IVUS guidance versus angiography guidance such as major bleeding emerged (42% relative risk reduction in favor of IVUS guidance). Beyond the lack of randomization, there were no prespecified criteria of IVUS-guided optimization of stent deployment precluding new knowledge of how IVUS could inform the procedure to improve results. Similarly, the reader is not informed whether the reading of IVUS acquisitions was correct (eg, some physicians participating had no experience with IVUS according to the authors) and whether corrective measures resulted in the anticipated changes, because neither the analysis of the pullbacks nor the final angiography were reported. Notwithstanding, IVUS did result in a larger stent or balloon diameter in 38%, a longer stent in 22%, or higher inflation pressures in 23% of cases, suggesting that IVUS might have improved stent underexpansion and malapposition.

What Are the Mechanistic Explanations for the Observed Clinical Benefit?

In the context of an observational study design, it is prudent to support findings by plausible mechanistic explanations of the observed benefits. Clinical end points related to device implantation potentially influenced by IVUS guidance were only affected, in part, in the present study. Although the data do indicate a benefit in terms of target vessel myocardial infarction and target lesion revascularization, no difference was noted in terms of definite stent thrombosis—the end point most likely to be affected by IVUS guidance. A reduction in target vessel myocardial infarction unrelated to differences in the risk of definite stent thrombosis raises the question of alternative explanations and could be potentially explained by the progression of de novo coronary artery disease in untreated regions of the target vessel. Theoretically, IVUS guidance may have improved lesion coverage and reduced geographical miss. Consistent with this hypothesis, total stent length was longer in the IVUS group, and a reduction in geographical miss has been shown to improve outcomes in some analyses.[13] A detailed review of all coronary angiograms and IVUS sequences of the target vessel before and after stent implantation could have substantiated the presence of vulnerable lesions in the vicinity of stented vessel segments owing to incomplete lesion coverage.

Which Patients Are Likely to Benefit From IVUS-Guided PCI?

Previous reports observed a benefit from IVUS-guided PCI particularly in left main interventions.[6] ADAPT DES suggests that IVUS guidance may be particularly beneficial among patients with complex lesion characteristics including left main, bifurcations, and multivessel disease, and among patients with acute coronary syndrome, as well, particularly those presenting with ST-elevation myocardial infarction who are undergoing primary PCI. The latter patients have a high risk for recurrent ischemic adverse events,[14] which may explain why IVUS-guided PCI yielded the largest benefit in this subgroup. Optimal selection of stent size and landing zone is challenging during primary PCI because of the presence of thrombus and vessel spasm, and may be facilitated by using intracoronary imaging. Whether IVUS, which falls short of differentiating thrombus from other tissue types, is the ideal imaging technology for the assessment of thrombotic lesions remains unclear. The importance of adequate stent sizing and lumen expansion during PCI has been previously reported by the same group of investigators in the HORIZON-AMI IVUS substudy.[15] Contrary to the observations in ADAPT DES, IVUS guidance during primary PCI was not an independent predictor of mortality or definite stent thrombosis in the Korea Acute Myocardial Infarction Registry including 2127 patients with IVUS guidance and 8235 control patients.[16]

In the ADAPT DES registry, all patients with acute coronary syndrome were treated with clopidogrel instead of the more potent novel P2Y12 inhibitors ticagrelor and prasgurel.[17,18] It remains to be shown if and to what degree the optimization of stent deployment by intracoronary imaging would be camouflaged by the superseding impact of potent antithrombotic therapy.

Future Perspectives

It is somewhat disconcerting that after >20 years of intravascular imaging, there remains a void of convincing data to support its use in routine clinical practice. Intuitively, any imaging technique with superior resolution, improved tissue characterization, and easier interpretation should advance both diagnosis and treatment. In addition, novel devices such as bioresorbable coronary scaffolds require meticulous attention to lesion characteristics, lesion preparation, and accurate deployment, which may be facilitated by intracoronary imaging. Moreover, long-term arterial healing and monitoring of the resorption process after scaffold implantation is best achieved by intracoronary imaging. The hope remains that research in this field and the use of new technologies such as optical coherence tomography— a light-based modality with 10 times higher resolution than IVUS—will provide convincing outcome data for the more ubiquitous use of intracoronary imaging during coronary interventions. Until then, angiography-guided PCI will remain the standard of care that may be supplemented by intracoronary imaging in selected high-risk patients and a lesions subset such as those deriving the greatest benefit in ADAPT DES.

Disclosures

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